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EXAMINER	
BRISTOL, LYNN ANNE	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,117	YANG ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-49 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-49 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-49 are all the pending claims subject to lack of unity restriction/election.

2. Effective as of January 22, 2007 the Office decision to rescind the waiver of the requirements for restriction of nucleotide sequences set forth in the 1996 Notice now considers each polynucleotide molecule for independence, relatedness, distinction and burden as for claims to any other type of molecule (see Off. Gaz. (Mar 27, 2007)). Accordingly, individual polypeptide or nucleotide sequences have been speciated as indicated below.

Lack of Unity: Restriction

3. Restriction is required under 35 U.S.C. 121 and 372.

The claims of the present application relate to methods of using an oligonucleotide probe for targeting nucleic acid structures (e.g., RNA) comprising a linked energy donor moiety and a linked energy acceptor moiety interposed by a nucleotide sequence which forms a stem-loop hairpin with the nucleic acid structure.

In assessing whether the requirements of unity of invention of an application are met, identification of the technical features that each solution to a technical problem contributes over the prior art (special technical features) must be made. If then a technical relationship between the solutions, involving one or more of the same technical features, can be recognized, the requirements of unity of invention are said to be met.

Methods of using a molecular beacon probe or the oligonuclotide probe of Claim 1 to detect tumor marker RNA were already known before the priority date of the present application. For example, Polstra et al. (BMC Infect. Dis. 2: 18-28 (2002)) discloses oligodeoxyribonucleotide probes labeled with a fluorescent dye on one end and a fluorescent quencher on the end, where the oligodeoxyribonucleotide forms a stem-loop hairpin structure with the target substrate mRNA upon hybridization. Polstra discloses detection of human herpes virus-8 RNA is directly correlated with pathogenesis of Kaposi's saracoma, thus the human herpes virus-8 RNA corresponds as a tumor marker. Thus, the technical feature of Claim 1 was not a contribution over the prior art at the time of the application filing.

4. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. The resulting separate inventions, as presently identified, have been grouped according to the order in which they have been claimed.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-17, drawn to a method of detecting at least one tumor marker RNA in a sample comprising treating the sample with an oligonucleotide comprising a linked energy donor moiety and a linked energy acceptor moiety interposed by a nucleotide sequence which forms a stem-loop hairpin with a target sequence, and detecting, identifying or quantitating hybridization with the sequence in order to detect, identify or quantitate the presence of the mRNA sequence.

Group II, claim(s) 18-21, drawn to a method of detecting a mutant gene in a tumor cell comprising treating the tumor cell with an oligonucleotide comprising a linked energy donor moiety and a linked energy acceptor moiety interposed by a nucleotide sequence which forms a stem-loop hairpin with a mutant gene sequence, and detecting,

identifying or quantitating hybridization with the gene in order to detect, identify or quantitate the presence of the mutant gene.

Group III, claim(s) 22 and 23, drawn to a method of monitoring alterations in gene expression in viable cells comprising treating the cell with an oligonucleotide comprising a linked energy donor moiety and a linked energy acceptor moiety interposed by a nucleotide sequence which forms a stem-loop hairpin with a particular gene sequence, and detecting, identifying or quantitating hybridization with the sequence in order to detect, identify or quantitate the alteration in gene expression.

Group IV, claim(s) 24-35, drawn to a method of monitoring presence or progression of breast cancer in a subject comprising treating a sample with an oligonucleotide comprising a linked energy donor moiety and a linked energy acceptor moiety interposed by a nucleotide sequence which forms a stem-loop hairpin with a breast cancer marker gene sequence, and detecting, identifying or quantitating hybridization with the sequence in order to detect, identify or quantitate the sequence.

Group V, claim(s) 36-44, drawn to a method of monitoring presence or progression of pancreatic cancer in a subject comprising treating a sample with an oligonucleotide comprising a linked energy donor moiety and a linked energy acceptor moiety interposed by a nucleotide sequence which forms a stem-loop hairpin with a pancreatic cancer marker gene sequence, and detecting, identifying or quantitating hybridization with the sequence in order to detect, identify or quantitate the sequence.

Group VI, claim(s) 45-47, drawn to a method of detecting cancerous cells in a sample comprising treating the sample with an oligonucleotide comprising a linked energy donor moiety and a linked energy acceptor moiety interposed by a nucleotide sequence which forms a stem-loop hairpin with a cancer-specific marker gene sequence, and detecting, identifying or quantitating hybridization with the sequence in order to detect, identify or quantitate the presence of the sequence.

Group VII, claim(s) 48, drawn to a diagnostic kit for monitoring presence or progression of pancreatic cancer in a subject.

Group VIII, claim(s) 49, drawn to a diagnostic kit for detecting alteration in gene expression in viable cells.

5. As no technical feature(s) can be distinguished which, in light of the prior art, could be regarded as special technical features on which a unifying concept could be

based, there is no single inventive concept underlying the plurality of claimed inventions.

6. Six different methods are presented in Groups I-VI. The Inventions of Groups I-VI differ in the method objectives, method steps and parameters and in the reagents and/or doses and/or schedules used, response variables, assays for end products and/or results, and criteria for success. The examination of all groups would require different searches in the U.S., international and foreign patent literature and the scientific literature and would require the consideration of different patentability issues. Thus Inventions I-VI are separate and distinct and are patentably distinct.

7. Two different products are presented in Groups VII and VIII. The Inventions of Groups VII and VIII do not share a common property or activity and do not share common core structures. The kit components of Groups VII and VIII are used for different method conditions and the kit of Group VII is not disclosed as being usable under the conditions for the kit of Group VIII. Thus Inventions of Groups VII and VIII are patentably distinct.

8. Inventions of Group VII and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the method for monitoring presence or progression of pancreatic cancer in a subject can be

practiced with a materially different reagent such as a labeled antibody recognizing the pancreatic cancer marker protein.

9. Inventions of Group VIII and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the method for monitoring alterations in gene expression in viable cells can be practiced with a materially different reagent such as PCR amplification or Western blotting for expressed protein levels of the particular gene.

10. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

11. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Election of Species Requirement

12. If Group I, IV or V is elected, then species (tumor marker) below must be elected as applicable. This application contains claims directed to the following patentably distinct species of the claimed invention:

Specie A) survivin

Specie B) cyclin D1

Specie C) Her2/neu

Specie D) a mutant K-ras

Specie E) chymotrypsinogen

Specie F) basic fibroblast growth factor

Specie G) carcinoembryonic antigen

Specie H) prostate specific antigen

Specie I) alpha-fetal protein

Specie J) beta-2-microglobulin

Specie K) bladder tumor antigen

Specie L) chromogranin A

Specie M) neuron-specific enolase

Specie N) S-100

Specie O) TA-90

Specie P) tissue polypeptide antigen

Specie Q) human chorionic gonadotropin

Specie R) EGF receptor

Species A-R are structurally and functionally distinct antigens, each well recognized in the art as being expressed on different cell types, having different protein sequences, different cognate ligands and signal interactions in cell pathways. One skilled in the art could consult any commercial protein sequence website (e.g., UniProtKB/SwissProt) which lists this information. In addition, The Human Protein Reference Database (HPRD.org) describes the tissue expression patterns, structural and functional properties and any disease correlates for these proteins. The species are not obvious variants or overlapping, and because searching the databases for each of the species is not co-extensive, speciation for examination purposes is proper.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 1 and 3-17 (Group I) are generic to species A-Q; Claims 24 and 26-35 (Group IV) are generic as to species A-C, F, G and R; and Claims 36 and 38-43 (Group V) are generic as to species A, D and G.

13. If Group I, II, IV or V is elected, then species (oligonucleotide) below must be elected as applicable. This application contains claims directed to the following patentably distinct species of the claimed invention:

Specie A) SEQ ID NO:1

Specie B) SEQ ID NO:2

Specie C) SEQ ID NO:3

Specie D) SEQ ID NO:4

Specie E) SEQ ID NO:5

Specie F) SEQ ID NO:6

Specie G) SEQ ID NO:7

Specie H) SEQ ID NO:8

Specie I) SEQ ID NO:9

Specie J) SEQ ID NO:10

Specie K) SEQ ID NO:11

Specie L) SEQ ID NO:12

Specie M) SEQ ID NO:13

The oligonucleotides are patentably distinct because they are unique structures composed of different nucleotide residues. The search of any particular sequence is not coextensive with the search of any other different sequence, one specific sequence, or one specific combination of sequences, and a reference against one sequence is not necessarily a reference against any other sequence.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 1-8, 10, 12, 14 and 16 (Group I) are generic to species A-M; Claims 18-20 (Group II) are generic to species G, H and K-M; Claims 24-30, 32, and 34 (Group IV) are generic to species A-F and I; and Claims 36-41 and 43 (Group V) are generic to species A, B, G-I and K-M.

14. If Group VI is elected, then species (cancer cell origin) below must be elected as applicable. This application contains claims directed to the following patentably distinct species of the claimed invention:

Specie A) breast

Specie B) pancreas

Specie C) ovarian

Specie D) prostate

Specie E) colorectal

Specie F) hepatocellular

Specie G) multiple myeloma

Specie H) lymphoma

Specie I) bladder

Specie J) medullary carcinoma of the thyroid

Specie K) neuroendocrine tumors

Specie L) carcinoid tumors

Specie M) testicular

Specie N) gestational trophoblast neoplasms

Specie O) lung

Specie P) melanoma

Specie Q) stomach

The species of cancer do not share a common utility nor do they have a substantial structural feature common amongst them. Each of the cancers can originate from any number of different cell types (e.g., epithelial, endothelial or mesothelial). Also, the cancers being associated with different organs are nevertheless, under the influence of different growth factors and hormones. Additionally, numerous studies have shown that receptor density and affinity for different diagnostic biomolecules is highly variable amongst different tissues and organs, in addition to there being differences to the extent to which biomolecules are able to penetrate cancers. Thus, species A-Q are patentably distinct cancers with respect to a detecting method.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 45 and 46 are generic to species A-Q.

15. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LAB

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